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Sequential Catalytic Modification of the Lignin α-Ethoxylated β-O-4 Motif To Facilitate C−O Bond Cleavage by Ruthenium-Xantphos Catalyzed Hydrogen Transfer

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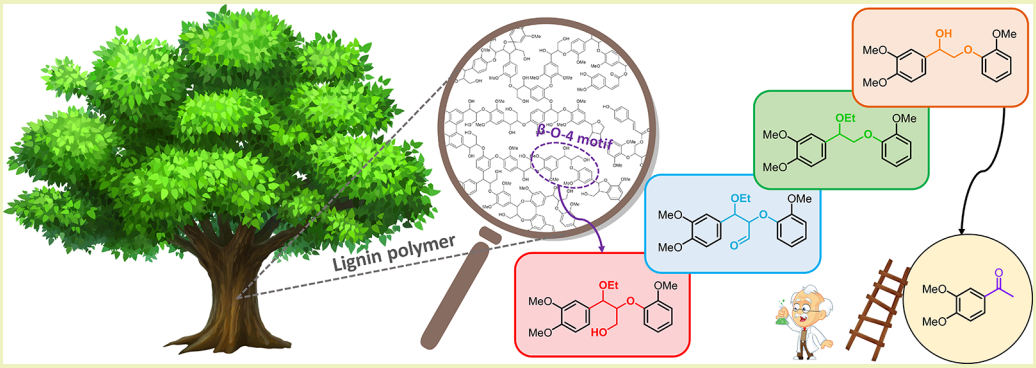
Supporting Information



ABSTRACT: Lignin is an abundant natural biopolymer that has the potential to act as a renewable feedstock for valuable aromatic compounds via selective catalytic depolymerization. In recent years, elegant, mild, catalytic hydrogen neutral C−O bond cleavage methodologies have been developed on model compounds yielding acetophenone derivatives. However, none of these have been reported to be effective once applied to lignin. One of the reasons for this is the highly functionalized nature of the native lignin β-O-4 motif, which is often not taken into account in the β-O-4 model compounds used for methodology development. In this work, we demonstrate the development of a stepwise modification protocol on lignin β-O-4 model compounds to overall yield a partially defunctionalized β-O-4 motif. This was achieved by making use of an α-ethoxylated β-O-4 motif that is readily available from ethanosolv extraction of lignocellulosic biomass. This specific motif allowed us to apply selective copper catalyzed aerobic oxidation and subsequent rhodium catalyzed decarbonylation of the primary hydroxyl group in the γ position. The obtained partially defunctionalized β-O-4 lignin motif allowed effective homogeneous ruthenium catalyzed hydrogen neutral C−O bond cleavage (>99% of 3,4-dimethoxyacetophenone and >99% of guaiacol). The stepwise modification strategy was extended to walnut ethanosolv lignin, demonstrating that the specific structural motifs are accessible from such a readily available lignin. Overall, this work illustrates that the structure of lignin can be strategically modified to allow access to otherwise inaccessible specific aromatic compounds via selective depolymerization methodologies.

KEYWORDS: *Lignin, Aerobic oxidation, Decarbonylation, Hydrogen borrowing, Depolymerization, Ethanosolv*

INTRODUCTION

Lignin is a key component of lignocellulosic biomass making up approximately 15−35% of the total weight depending on the biomass source.[1−4] To realize economically viable biorefinery schemes, valorization of the lignin component is essential.[5,6] However, currently lignin is primarily used as a low-value fuel to provide heat for pulping processes targeting carbohydrates. Higher value could be extracted from lignin by its conversion into desirable industrial chemicals. As the most abundant natural aromatic biopolymer, lignin would ideally serve as a renewable feedstock for key aromatic chemicals. To achieve this, significant research effort has been devoted to developing integrated catalytic methodology to deconstruct lignin to specific aromatic (mostly phenolic) compounds.[7−16] As the most abundant linkage motif in native lignin, selectively cleaving the β-O-4 motif (typically over 50% of linking motifs) is crucial.[17] One effective depolymerization approach relies on the transformation of the benzylic α-OH of the β-O-4 motif, which activates the C−O bond for cleavage.[18] This can be achieved by selective oxidation of the benzylic alcohol and subsequent depolymerization for which several procedures have been developed leading to different sets of monomeric products.[19−26] Bergman and Ellman pioneered such activation of the lignin β-O-4 motif and its subsequent C−O cleavage using model compounds.[27] They achieved the former by dehydrogenation of the benzylic alcohol using a homogeneous

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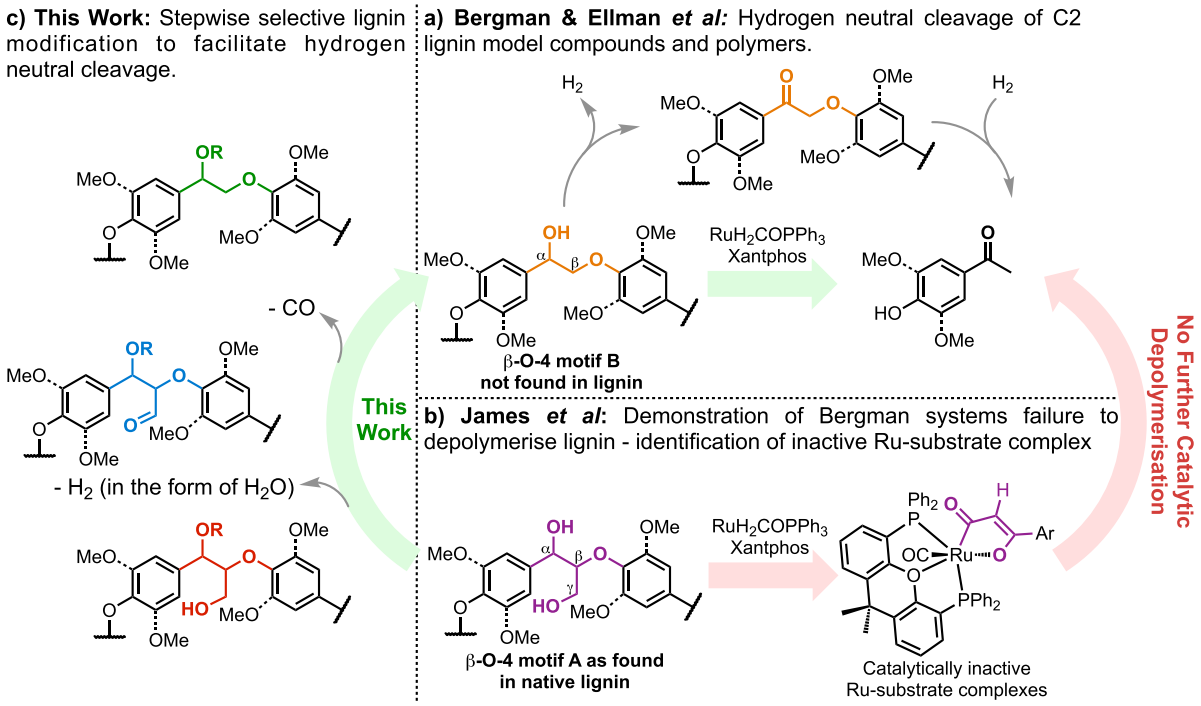

Figure 1. (a) Depolymerization/cleavage of C2-β-O-4 motif B containing dimeric and polymeric model compounds using hydrogen borrowing developed by Bergman et al.[27] (b) Mechanistic studies by James et al. showing chelation of C3-β-O-4 motif A causing ineffective catalytic C−O bond cleavage.[36] (c) Outline of the lignin modification steps presented in this work that convert the C3-β-O-4 motif A to C2-β-O-4 motif B facilitating hydrogen neutral depolymerization.

ruthenium-Xantphos catalyst and the latter by utilizing the released equivalent of hydrogen for the C−O bond reduction by the same catalyst (Figure 1a). This hydrogen borrowing method[28−31] is very elegant as it uses only a catalyst as additive, is neutral in hydrogen featuring an overall 100% atom efficiency and yields a chemically versatile ketone-containing depolymerization product. This methodology has the advantage over recently popular acidic, oxidative and reductive methods for lignin depolymerization that require the addition of stoichiometric sacrificial reagents either for depolymerization or trapping of reactive intermediates such as the use of hydrogen or sacrificial hydrogen donating agents.[20,21,32−35] Nevertheless, the hydrogen borrowing methodology was only truly effective on simplified C2-β-O-4 dimeric and polymeric model systems (β-O-4 motif B, Figure 1a). Detailed mechanistic studies by the group of James showed that this method cannot operate effectively when applied to lignin.[36] They found, using model compounds, that the γ-hydroxy group in the native lignin β-O-4 motif A chelates to the ruthenium-Xantphos complex, trapping and thus deactivating the ruthenium catalyst (Figure 1b). Since the publication by Bergman and Ellman in 2010, many catalytic systems were developed that can catalyze the same depolymerization reaction sequence on the structurally simplified C2-β-O-4 model compounds representing β-O-4 motif B,[37−42] but none of these have been reported to be able to effectively depolymerize lignin.

In this work, we present a different approach. Instead of developing another catalytic system, we demonstrate how, through a series of carefully chosen catalytic lignin modification reactions, it is possible to modify the native lignin β-O-4 motif A so that for the first time, depolymerization of lignin via hydrogen borrowing yields functionalized acetophenones. The overall removal of the problematic γ-carbinol group is the key structural transformation effectively converting lignin to a C2-β-O-4 polymer (β-O-4 motif B). Thus, the native β-O-4 motif A is transformed into the unnatural β-O-4 motif B which does not interfere with hydrogen neutral depolymerization via hydrogen borrowing (Figure 1c). Conceptually, no addition of external reagents is required for this transformation if achieved via acceptorless dehydrogenation and decarbonylation releasing the γ-carbinol group as synthesis gas. This could be a significant advantage over reductive fractionation or lignin depolymerization methods that require hydrogen or sacrificial hydrogen donors.[43] As a proof of concept, this transformation is achieved via three novel β-O-4 modification steps which were developed using model compounds. (1) Selective oxidation of the primary alcohol at the γ position in the β-O-4 motif A to an aldehyde. This was previously reported to be unselective or lead to product decomposition via retro aldol reactions.[44,45] To avoid structural decomposition we were inspired by the work of Westwood et al, who used a selectively α-butoxylated β-O-4 motif A, that can be obtained from butanosolv extraction of lignocellulosic biomass, to achieve selective primary oxidation to the carboxylic acid.[46] Here, we utilized an α-ethoxylated motif (accessible via ethanosolv extraction of lignocellulosic biomass) in combination with copper catalyzed aerobic oxidation[47−49] to install an aldehyde functionality on the γ position of β-O-4 motif A. (2) Catalytic decarbonylation to remove the aldehyde functionality and yield the partly defunctionalized C2-β-O-4 motif B containing an α-ethoxy group. This was achieved using a rhodium-dppp homogenuous catalyst.[50,51] (3) Finally, the α-ethoxy group was transformed back to a hydroxyl group by acid catalyzed α-hydroxylation to obtain the target C2-β-O-4 motif B that

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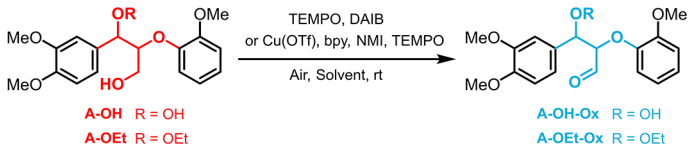

Entry	Substrate	Catalyst	Time	Solvent
1	A-OH	Cu(OTf) (15 mol%)/bpy/NMI/TEMPO	24h	MeCN
2	A-OH	TEMPO (10 mol%)/DAIB	24h	MeCN
3	A-OEt	TEMPO (10 mol%)/DAIB	24h	MeCN
4	A-OEt	TEMPO (10 mol%)/DAIB	43h	MeCN
5	A-OEt	TEMPO (10 mol%)/PS-DAIB	100h	MeCN
6	A-OEt	Cu(OTf) (5 mol%)/bpy/NMI/TEMPO	24h	MeCN
7	A-OEt	Cu(OTf) (5 mol%)/bpy/NMI/TEMPO	96h	MeCN
8	A-OEt	Cu(OTf) (10 mol%)/bpy/NMI/TEMPO	48h	MeCN
9	A-OEt	Cu(OTf) (10 mol%)/bpy/NMI/TEMPO	96h	MeCN
10	A-OEt	Cu(OTf) (15 mol%)/bpy/NMI/TEMPO	24h	MeCN
11	A-OEt	Cu(OTf) (15 mol%)/bpy/NMI/TEMPO	67h	MeCN
12	A-OEt	Cu(OTf) (20 mol%)/bpy/NMI/TEMPO	24h	MeCN
13	A-OEt	TEMPO (10 mol%)/PS-DAIB	156h	1,4-dioxane
14	A-OEt	Cu(OTf) (15 mol%)/bpy/NMI/TEMPO	24h	MeCN/trace water
15	A-OEt	Cu(OTf) (15 mol%)/bpy/NMI/TEMPO	24h	MeCN:1,4-dioxane=9:1
16	A-OEt	Cu(OTf) (15 mol%)/bpy/NMI/TEMPO	24h	MeCN:DMSO=9:1

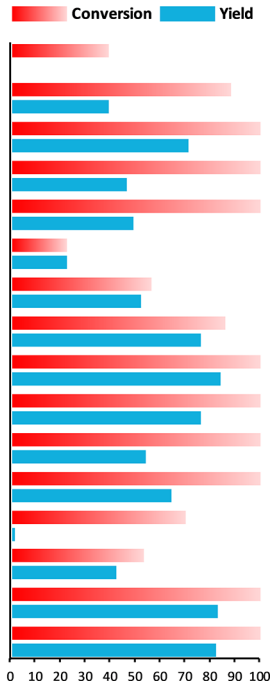

Figure 2. Overview of selective oxidation reactions of the γ position of β-O-4 model compounds. Reaction conditions: 25 mg of substrate, with either a 1:1:2:1 ratio of TEMPO:bpy:NMI:Cu(OTf) (e.g., 5 mol % Cu, other components were adjusted to the copper amount to keep the same ratio), DAIB:TEMPO 1.3:0.1, or PS-DAIB:TEMPO 1.3:0.1 (10 mol % TEMPO) as catalyst, performed under aerobic atmosphere at room temperature in 3 mL of solvent as shown, yield and conversion determined by quantitative NMR using 1,4-dinitrobenzene as external standard.

allows for effective depolymerization via hydrogen borrowing. After successful application on model compounds, this sequence of reactions was then studied on lignin to yield a modified lignin structure that allows for acetophenone type depolymerization products via the above-mentioned Ru/Xantphos catalyzed hydrogen borrowing reaction.

RESULTS AND DISCUSSION

Selective γ-Oxidation of β-O-4 Motif A. Our defunctionalization strategy of the native β-O-4 motif A via decarbonylation relied on the successful installment of an aldehyde at the γ position. Thus, initially two reported room temperature primary alcohol oxidation procedures were tested on model compound **A-OH**: (1) aerobic catalytic Cu(OTf)/bpy/TEMPO/NMI[47−49] and (2) TEMPO/DAIB,[52] both of which were previously tested on lignin model compounds.[44,53,54] However, in our hands, the reaction with procedure (1) gave conversion but none of the desired γ-aldehyde oxidation product, while (2) giving some desired product but with unsatisfactory selectivity (Figure 2 entries 1 and 2). Here, as previously reported,[20,44,45,55] the obtained aldehyde containing motif **A-OH-Ox** proved to be labile and show tendency decompose to give veratraldehyde and guaiacol via a retro-aldol reaction, both of which were indeed found as products in the reaction mixture. This instability also gave problems in attempts to isolate **A-OH-Ox**, leading to decomposition during chromatography to yield new veratraldehyde and guaiacol impurities.

Recently, it was shown that butanosolv extraction of different biomass sources can be tuned to yield a modified lignin structure in which the lignin β-O-4 motif is extensively α-butoxylated.[46,56] This α-butoxylated β-O-4 motif A allows for new selective chemistry due to the "protected" benzylic position as demonstrated in accordingly modified model compounds as well as butoxylated lignin itself.[57] Among the selective modification reactions enabled by the butoxylation of β-O-4 motif A was selective oxidation chemistry to yield a carboxylic acid in the γ position.[46] Ethanosolv lignin is more commonly practiced compared to butanosolv extraction and has been applied on large scale.[58] As for butanosolv extraction, also ethanosolv extraction can yield lignin with high β-O-4 content[59] along with high α-ethoxylation when conditions are carefully tuned.[60] Therefore, we sought to make use of an α-ethoxylated β-O-4 motif A to allow for the selective transformation on the γ-hydroxy group to the corresponding aldehyde. Using a model compound (**A-OEt**) to reflect this structural motif, selective primary alcohol oxidation to the γ-aldehyde (**A-OEt-Ox**) was attempted. Using TEMPO/DAIB, **A-OEt-Ox** was obtained in high selectivity when the reactions were not run in excess of 24 h (Figure 2 entries 3 and 4). The use of the α-ethoxylated β-O-4 model compound gave a far higher selectivity to the aldehyde product compared to the use of **A-OH**, highlighting again the potential for this structure for selective chemical modification of the β-O-4 motif. However, the decarbonylation step suffered significantly from impurities that were the result from this oxidation methodology. In

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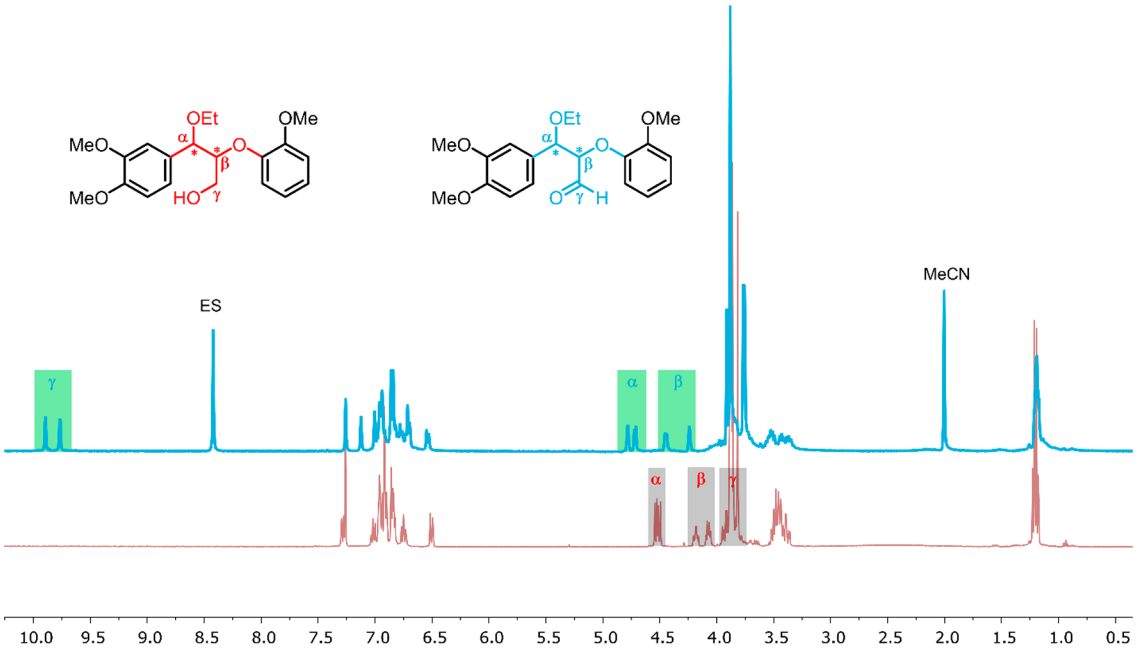

Figure 3. ^{1}H NMR overlay of purified **A-OEt** (red, bottom) and crude **A-OEt-Ox** (blue, top) obtained from the Cu (15 mol %)/bpy/NMI/TEMPO catalyzed aerobic oxidation reaction (Figure 2 entry 10). The signals belonging to the α-, β-, and γ-hydrogens of **A-OEt** and **A-OEt-Ox** are highlighted. *Chiral centers, both **A-OEt** and **A-OEt-Ox** are present as two diastereomers in a 1:1 ratio according to ^{1}H NMR.

particular, iodobenzene released from DAIB (Supporting Information (SI) Scheme S1) proved hard to completely remove and was found in control decarbonylation reactions using benzaldehyde to acts as an inhibitor for the decarbonylation (SI Scheme S3). This is likely caused by iodobenzene oxidatively adding to the metal complex leading to an inactive iridium complex. Using a polystyrene immobilized version of DAIB (PS-DAIB) the deactivation problem could be overcome as the iodobenzene being bound to polystyrene could easily be removed from the reaction mixture. However, PS-DAIB did not give satisfactory selectivity due to a significant slower reaction (Figure 2 entry 5), which increased the ethanol elimination side reaction leading to an α,β-unsaturated aldehyde.[44] Additionally, this methodology appears to be sensitive to the solvent used (Figure 2 entry 13). For these reasons, Cu/bpy/NMI/TEMPO catalyzed aerobic oxidation was attempted as an alternative.[47−49] This method uses oxygen as oxidant and thus avoids the use of DAIB as stoichiometric oxidant, which gives a major sustainability advantage. Additionally, the catalyst components could readily be separated from the product by an aqueous wash, leaving typically only trace quantities of TEMPO in the crude product mixtures. Additionally, advances in the development of immobilized TEMPO derivatives have the potential to offer recyclability which is not achieved in this work.[61,62] Satisfyingly, this oxidation methodology led to excellent selectivity when applied to **A-OEt**, in particular when the catalyst loading was increased 3-fold (Figure 2 entries 6 and 10). After 24 h, 76% yield of **A-OEt-Ox** was obtained as determined by ^{1}H NMR using 1,4-dinitrobenzene as an external standard, showing highly selective oxidation to the desired product. Longer reaction time as well as increased amount of catalyst led to unknown decomposition products in addition to traces of veratraldehyde and the α,β-unsaturated aldehyde (Figure 2 entries 11 and 12). The crude ^{1}H NMR spectra were actually a lot cleaner than the yield of **A-OEt-Ox** indicated by the use of the external standard (Figure 3). As shown, the product's ^{1}H NMR shifts related to the α-, β-, and γ-hydrogens are obvious and clearly distinguishable and no starting material or other products are present in significant quantities. Therefore, the reaction shown in entry 10 of Figure 2 was also run with an internal standard, showing a 10% higher yield of **A-OEt-Ox** (86%), indicating that the yields in Figure 2 are an underestimation and the procedure performs excellently.

The solvent compatibility was investigated as acetonitrile, which according to literature is the best solvent for this reaction,[48] was anticipated to not satisfactorily solubilize lignin. In this case, better selectivities were achieved using both 1,4-dioxane and DMSO mixtures (83% and 82% respectively), which are both excellent solvents for lignin (Figure 2 entries 15 and 16). Importantly, it was found that water did significantly reduce the reaction rate, meaning that the lignin substrate should be appropriately dried before use (Figure 2 entry 14). Decreased catalyst loading to 5 mol %, although being highly selective, gave lower conversion and yield even with extended reaction times of up to 96 h (Figure 2 entries 6 and 7). Reactions of 96 h with 10 mol % catalyst loading produced results comparable with those observed with 15 mol % at 24 h (Figure 2 entries 9 and 10). With this methodology in hand, we felt confident to have an effective method to install a γ-aldehyde in the lignin β-O-4 motif as well as a method to synthesize **A-OEt-Ox** to investigate the decarbonylation methodology.

Decarbonylation of A-OEt-Ox to β-O-4 Motif B (B-OEt). Next, the decarbonylation of **A-OEt-Ox** was investigated to yield the defunctionalized model compound **B-OEt**. A reported, robust iridium-triphenyl phosphine (PPh_3) catalytic system was initially selected as it is suitable for decarbonylation of a wide range of aldehydes with different functionalities and performs excellently in 1,4-dioxane.[63] Additionally, this catalyst was previously applied in lignin product defunctionalization and thus showed compatibility with lignin.[35] However, when

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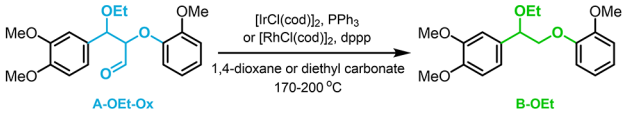

Entry	Catalyst	Time	Temperature (°C)
1	$[IrCl(cod)]_2$ (5 mol%)/PPh_3	24h	170
2	$[IrCl(cod)]_2$ (10 mol%)/PPh_3	24h	170
3	$[IrCl(cod)]_2$ (15 mol%)/PPh_3	24h	170
4	$[IrCl(cod)]_2$ (5 mol%)/PPh_3	24h	185
5	$[IrCl(cod)]_2$ (10 mol%)/PPh_3	24h	185
6	$[RhCl(cod)]_2$ (2.5 mol%)/dppp	24h	175
7	$[RhCl(cod)]_2$ (5 mol%)/dppp	24h	185
8	$[RhCl(cod)]_2$ (10 mol%)/dppp	24h	185
9	$[RhCl(cod)]_2$ (5 mol%)/dppp	9h	200
10	$[RhCl(cod)]_2$ (5 mol%)/dppp	24h	200
11*	$[RhCl(cod)]_2$ (2.5 mol%)/dppp	24h	200

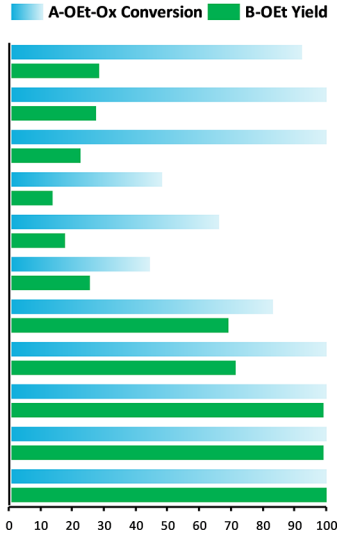

Figure 4. Selected data obtained from decarbonylation reactions of **A-OEt-Ox** to **B-OEt**. Reaction conditions: 15 mg of substrate, $[RhCl(cod)]_2$ 2.5−10 mol %, 2:1 dppp:Rh, or $[IrCl(cod)]_2$ 5 mol %, 1:1 PPh_3:Ir as catalyst (e.g., 5 mol % Rh or Ir precursor, other components were adjusted to the metal amount to keep the same ratio), 170−200 °C in 1 mL of solvent, yield and conversion determined by GC-FID using *n*-decane as internal standard. *Solvent = diethyl carbonate.

A-OEt-Ox in 1,4-dioxane was heated to 120 °C in the presence of a catalytic amount of $[IrCl(cod)]_2$ (5 mol %) and PPh_3 (10 mol %) for 24 h, no decarbonylation product (**B-OEt**) was found. Increasing the temperature to 150 °C did give traces of **B-OEt**, which increased to 28% yield at 170 °C but with 92% conversion of **A-OEt-Ox** as determined by GC-FID (Figure 4 entry 1, additionally these reactions were monitored in time and the full data set shown in Table S1). Thus, the selectivity was unsatisfactory and many other products were observed. The main side-product that could be identified was a vinyl ether product that is obtained from ethanol elimination from **B-OEt**. This product can also be the result of the decarbonylation of the α,β-unsaturated aldehyde obtained from ethanol elimination from **A-OEt-Ox**. No distinction between these two pathways could be made. It was previously reported that elimination can be catalyzed by bases and thus uncomplexed triphenylphosphine could be acting as a base promoting the formation of the α,β-unsaturated aldehyde or the vinyl ether from **A-OEt-Ox** or **B-OEt**, respectively. Further increase of the catalyst loading did improve the conversion, however decreased the reaction selectivity, leading to lower B-OEt yield (Figure 4 entries 2 and 3). Curiously, an increase in temperature to 185 °C led to a drop in activity, which can be explained by rapid catalyst decomposition (Figure 4 entries 4 and 5).

Due to these unsatisfactory results with this iridium catalyst, the application of a published procedure using $[RhCl(cod)]_2$/1,3-bis(diphenylphosphino)propane (dppp) was attempted.[64] This procedure was previously used in the presence of lignin in order to decarbonylate depolymerization products and thus compatible with the many highly funcationalized motifs present in lignin. A reaction of **A-OEt-Ox** in 1,4-dioxane, heated to 175 °C in the presence of a catalytic amount of $[RhCl(cod)]_2$ (2.5 mol % Rh) and dppp (5 mol %) was monitored in time (Table S1 for full data). At 24 h, a conversion of 44% was observed but the yield and selectivity for **B-OEt** showed a significant improvement (25% and 55%, respectively, Figure 4 entry 6). Longer reaction times did not improve the yield significantly indicating catalyst decomposition or product instability. Increasing the temperature to 185 °C as well as doubling and quadrupling the catalyst loading led to a significantly improved conversion **A-OEt-Ox** to over 80% and 98% respectively, as well as the selectivity for **B-OEt** (83% and 71%, respectively, Figure 4 entries 7 and 8). In these reactions, the main side product was the α,β-unsaturated aldehyde with only traces of the vinyl ether, indicating that the former is not effectively decarbonylated by this catalytic system. Gratifyingly, increasing the temperature to 200 °C led to full conversion of **A-OEt-Ox** and near quantitative yield of **B-OEt** using 10 mol % Rh and 20 mol % dppp even after a 9 h reaction (Figure 4 entry 9). Running the reaction for longer (24 h) did not lead to a drop in yield, showing that the product is stable under these reaction conditions (Figure 4 entry 10). With green chemistry principles in mind, a series of greener and more sustainable solvents were also screened using veratraldehyde as model compound. Diethyl carbonate, anisole and diglyme showed comparable results with 1,4-dioxane (Table S2 for full data set). Also, full conversion of **A-OEt-Ox** to **B-OEt** was achieved even with half loading of catalyst in diethyl carbonate (Figure 4 entry 11). The difficult removal of the catalyst from the product mixture is one downside to this methodology. In the model compounds the metal complex and ligand were readily separated by flash chromatography, which was not a problem with **B-OEt** as it proved to be very stable. However, separation by column chromatography is not readily possible for lignin (vide infra).

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α-Hydroxylation of B-OEt to B-OH and Hydrogen Neutral C−O Bond Cleavage. With **B-OEt** in hand from the decarbonylation of model compound **A-OEt-Ox**, the next step was the "deprotection" of the α-benzylic position by exchange of the ethoxy group by a hydroxyl group (α-hydroxylation). This step is required to allow hydrogen abstraction from the benzylic alcohol of β-O-4 motif B to obtain the equivalent of hydrogen for the hydrogen neutral depolymerization to acetophenone derivatives. For this purpose, a previously reported[56,59] mild acid catalyzed α-hydroxylation procedure for β-O-4 motif A was applied to **B-OEt**, using a 2:1 mixture of 1,4-dioxane: water, 0.24 M HCl at 80 °C to obtain **B-OH** (Figure 5). The reaction, monitored in time, reached a

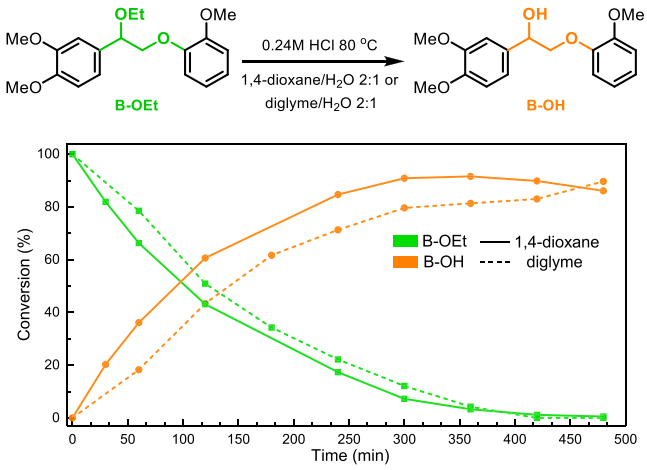


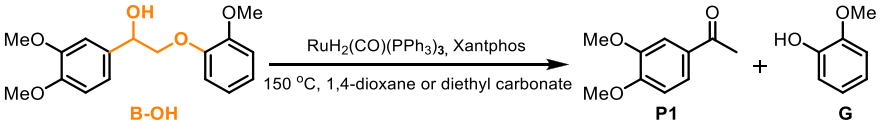
Figure 5. Reaction profile for the α-hydroxylation of **B-OEt** to **B-OH**. Reaction conditions: 0.09 mmol **B-OEt** 0.24 M HCl, 0.1 mmol 1,2,4,5-tetramethylbenzene (internal standard) at 80 °C in 4 mL of a 2:1 mixture of 1,4-dioxane: H_2O or 2:1 mixture of diglyme:H_2O.

maximum conversion of 91% after 6 h with a high mass balance. In principle, this is an equilibrium reaction explaining the peak conversion at 6 h at which point **B-OEt** and **B-OH** would be in a steady state equilibrium. This steady state equilibrium is a determined by the EtOH and H_2O concentrations as well as the relative stabilities of the compounds **B-OEt** and **B-OH**. At longer reaction times, some decomposition was seen indicating that **B-OH** is not fully stable under these acidic reaction conditions (Figure S1 for full graph). Some identified side products are in-line with acidolysis mixtures obtained in previous work from the β-O-4 motif B model compounds. Among these are the vinyl ether that is the result of dehydration of **B-OH** and guaiacol.[35,65−67] Removal of the solvent containing the released ethanol and then using the obtained product mixture to run the reaction in a fresh acidic 2:1 1,4-dioxane:water mixture in order to push for higher yields of **B-OH** were unsuccessful. This was again due to the formation of degradation products. Nevertheless, over 90% conversion with 100% selectivity was deemed satisfactory and **B-OH** could readily be obtained pure by column chromatography. The reaction was also found to be compatible with the more sustainable and environmentally benign solvent diglyme, reaching a **B-OH** yield of 90% upon allowing the reaction to run for 8 h.

To demonstrate the requirement of the α-hydroxylation step of **B-OEt** to **B-OH**, hydrogen neutral cleavage of **B-OEt** catalyzed by $RuH_2(CO)(PPh_3)_3$ and Xantphos was performed in 1,4-dioxane. No significant conversion was observed to acetophenone derivative **P1** and guaiacol (**G**). When this reaction was performed with **B-OH** as substrate, an excellent 91% yield of **P1** and 94% yield of **G** was obtained after 4 h (Table 1 entry 2), which is actually 10% higher compared to the yield reported by Bergman et al.[27] When the **A-OH** model compound was used as substrate, no significant formation of **P1** or **G** was observed. This confirms the literature precedent while demonstrating the overall effectiveness of the modification steps.[36] Upon adapting the procedure to use the greener and more environmentally benign solvent diethyl carbonate, the yields of **P1** and **G** improved further to >99% of both in 4 h with half of the catalyst loading (Table 1 entry 3 and 4).

Modification of Walnut Organosolv Lignin. With the model compounds results in hand the focus was shifted to extending the modification steps to application on a lignin sample. The first goal was to obtain a lignin sample with two key features: (1) high β-O-4 motif A content to allow us to clearly visualize the changes to the structure by HSQC NMR and for effective selective depolymerization (to release aromatic monomers from lignin it needs to be flanked by two cleavage linkages) and (2) high α-ethoxy incorporation, as the results from the model compound study clearly showed that this motif was essential for selective conversion of the primary alcohol in the γ position to the corresponding aldehyde. To achieve this, a 12 h, mild (80 °C) 1,4-dioxane/ethanol (1:1) organosolv extraction of milled walnut[59] using 0.24 M HCl was performed (Figure 6). With this method, 19.8 wt % (51% extraction efficiency) lignin (**LA**) was obtained with a high total β-O-4 content of which already 90% had the desired α-ethoxy containing β-O-4 motif. The lignin contained a 70:30 S:G ratio in accordance to the source material.[56,59] To increase the α-ethoxylated β-O-4 content in this lignin, **LA** was subjected to an acidic (0.24 M HCl) 1,4-dioxane/ethanol (1:4) mixture and heated to 80 °C for 4 h (Figure 6). From

Table 1. Hydrogen Neutral Ru/Xantphos Catalyzed C−O Bond Cleavage of B-OH to Acetophenone Derivative P1 and Guaiacol (G)



entry	time	solvent	catalyst	conv %	P1 yield %	G yield %
1	2 h	1,4-dioxane	$RuH_2CO(PPh_3)_3$ (5 mol %)/Xantphos (5 mol %)	100	85	86
2	4 h	1,4-dioxane	$RuH_2CO(PPh_3)_3$ (5 mol %)/Xantphos (5 mol %)	100	91	94
3	2 h	diethyl carbonate	$RuH_2CO(PPh_3)_3$ (2.5 mol %)/Xantphos (2.5 mol %)	100	83	80
4	4 h	diethyl carbonate	$RuH_2CO(PPh_3)_3$ (2.5 mol %)/Xantphos (2.5 mol %)	100	100	100

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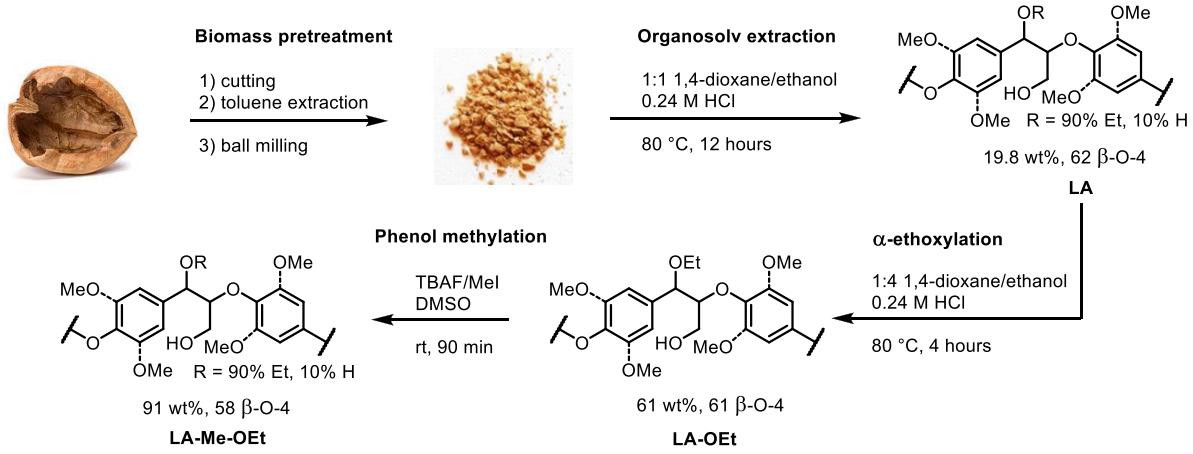

Figure 6. Method by which **LA**, **LA-OEt**, and **LA-Me-OEt** were obtained from walnut shells.

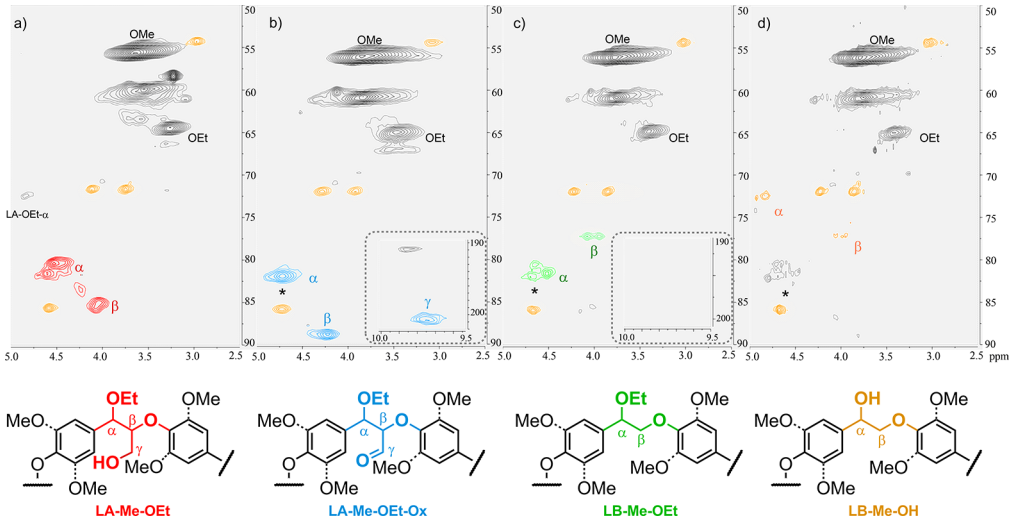

Figure 7. HSQC spectra (600 MHz, acetone-d_6 (a) or $CDCl_3$ (b–d)) of the linkage region of (a) **LA-Me-OEt** (starting lignin), (b) **LA-Me-OEt-Ox** (obtained by Cu/bpy/NMI/TEMPO catalyzed aerobic oxidation), (c) **LB-Me-OEt** (obtained by Rh/dppp catalyzed decarbonylation), and (d) **LB-Me-OH** (obtained by HCl catalyzed α-hydroxylation in 1,4-dioxane: water). *Overlap with unidentified impurity; signals corresponding to β–β linkages are colored yellow.

this reaction, 61 wt % of lignin was recovered containing a complete α-ethoxylated structure (**LA-OEt**) without a significant decrease in the total β-O-4 content (Figure 7a).

Initial oxidation reactions were performed with **LA-OEt** using the DAIB/TEMPO procedure but were unsuccessful. The ^{1}H NMR spectrum of the recovered lignin product showed a significant aldehyde signal, but the linkage region of the HSQC spectrum showed clear deconstruction of the original lignin structure. Most linkage signals were absent and thus the new aldehyde signal likely originates from vanillin/syringaldehyde type benzylic aldehydes in oligomeric lignin structures analogous to the veratraldehyde observed in the model compound reactions. A similar loss of linkage signals was observed previously when the same procedure was applied to birch ethanosolv lignin containing mostly non-α-ethoxylated β-O-4 motif A.[44] The focus was therefore shifted toward the aerobic Cu/bpy/NMI/TEMPO catalytic system that performed excellently in the model compound work (vida supra). However, application of this catalytic system on **LA-OEt** was initially also unsuccessful. No identifiable aldehyde peaks were observed in the HSQC spectrum of the recovered lignin product in the region where these were expected based on the model compound reactions. The poor performance was ascribed to two factors: (1) the reaction suffered from mediocre solubility of the lignin in acetonitrile and (2) the interference of phenol moieties that can undergo secondary oxidation reactions. To overcome both of these issues at once, an additional modification step was performed that removes the phenols by methylation using TBAF/MeI and which is known to improve solubility (Figure 6).[68,69] To monitor the reaction, phosphorus derivatization of the hydoxyl groups in lignin was performed and analyzed by ^{31}P NMR spectroscopy (Figures S5 and S7).[70,71] The spectra of the lignin before and after the methylation reaction, in which 91 wt % of lignin was recovered, clearly show the complete removal of the phenols. The signals related to the aliphatic hydroxyl groups mostly remained (a reduction of aliphatic hydroxy's from 1.69 to 1.58 mmol/g was measured), indicating that these groups were not methylated. The HSQC spectra of the obtained lignin (**LA-Me-OEt**) did show some α-hydroxylation of the β-O-4 motif A (10%) and a small loss in the total β-O-4 content (Table 2). **LA-Me-OEt** showed excellent solubility in acetonitrile and the mixture during aerobic Cu/bpy/NMI/TEMPO catalyzed oxidation of **LA-Me-OEt** remained homogeneous. Addition-

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Table 2. β-O-4 Content and recovery yield of LA-Me-OEt, LA-Me-OEt-Ox, LB-Me-OEt, and LB-Me-OH

	product			
	LA-Me-OEt	LA-Me-OEt-Ox	LB-Me-OEt	LB-Me-OH
β-O-4$_\alpha$[a]	58	42[b]	40[b]	10
β-O-4$_\beta$[a]	39	19	16	6
α:β ratio	1.5[b]	2.2	2.5	1.7
β–β_α[a]	10	10	10	12
recovery yield	91 wt %	84 wt %	96 wt %[c]	59 wt %

[a]As linkages per 100 aromatic units based on 2D HSQC. [b]Overlap with unknown impurity (see Figure 7). [c]Some catalyst is present in the sample.

ally, the catalyst components were readily separated from the lignin during the aqueous precipitation, filtration, and subsequent water washes that were performed to recover the lignin product (>80 wt % recovery in all oxidation attempts at a scale of 500 mg and higher. At a smaller scale the loss during work up accounts for a higher percentage). Shifting to a much greener methylation method is possible in the future work, as methylation of softwood kraft lignin with dimethyl carbonate has been successfully demonstrated.[72] In this oxidation attempt, aldehyde formation could clearly be observed by ^{1}H NMR of the recovered lignin after a reaction of 24 h, albeit the corresponding peak was low in intensity. When the catalyst loading was doubled and the temperature was increased to 40 °C, a significant increase in intensity of the aldehyde was observed in the ^{1}H NMR (Figure 8) as well as the HSQC spectrum (note: increased T1 relaxation time of 8.0 s was required for visualization of the aldehyde signal, Figure 7b) of the obtained lignin at the same reaction time.

A good match of the HSQC signals was observed when overlaying the spectrum with that of the model compound **A-OEt-Ox** (Figure S10) indicating that oxidation was successful and the desired aldehyde containing β-O-4 motif A was obtained. Nevertheless, the total β-O-4 content of this lignin (**LA-Me-OEt-Ox**) dropped considerably in this step (Table 2).

Next, **LA-Me-OEt-Ox** was exposed to Rh/dppp at 185 °C for 14 h, a little bit milder than optimal reaction conditions for the decarbonylation of model compound **A-OEt-Ox** to **B-OEt**. The obtained ^{1}H NMR (Figure 8) and HSQC spectrum (Figure 7c) of the recovered lignin product **LB-Me-OEt** (Table 2) showed a clear reduction of the aldehyde signal. Interestingly, following decarbonylation the solubility of the obtain lignin in deuterated acetone was decreased, conversely deuterated chloroform proved to be a good solvent for the obtained lignin material. The obtained HSQC spectrum also showed a similar pattern compared to that of the model compound **B-OEt** (Figure S13), indicating that a lignin with a β-O-4 motif B (**LB-Me-OEt**) had successfully been formed. Additionally, the release of carbon monoxide during the reaction was confirmed by GC-TCD analysis of a gas sample collected from the reaction after 9 h. One observation that was made in the HSQC spectrum is that the β-O-4 β-signal of **LB-Me-OEt** was much lower in intensity than expected compared to the β-O-4 α-signal (vide infra). The catalyst was difficult to remove from lignin, as it coprecipitated in water and did not dissolve in diethyl ether used for washing the lignin (see aromatic region of the full product HSQC spectrum, Figure S12). The obtained lignin was highly soluble in most other solvents that were tested, thus providing limited options for the removal of these catalyst components. To see whether these catalyst components could be removed in a subsequent step, the α-hydroxylation was performed with the crude **LB-Me-OEt** to obtain **LB-Me-OH** according to the procedure used to transform **B-OEt** to **B-OH**. In the product recovered after this reaction (Table 2), a new signal appeared upon HSQC analysis (Figure 7d) matching the α-signal for the representative model compound **B-OH** (Figure S15). However, a significant signal remained at the position for β-O-4 α-signal of **LB-Me-OEt**. For both **LA-Me-OEt-Ox** and **LB-Me-OEt**, a difference of intensity of the β-O-4 α-signal and the β-O-4 β-signal can be observed, which can be caused by a difference in relaxation time for the different nuclei. However, the typical α:β signal intensity ratio is in the order of 1.5 for all the steps up to the

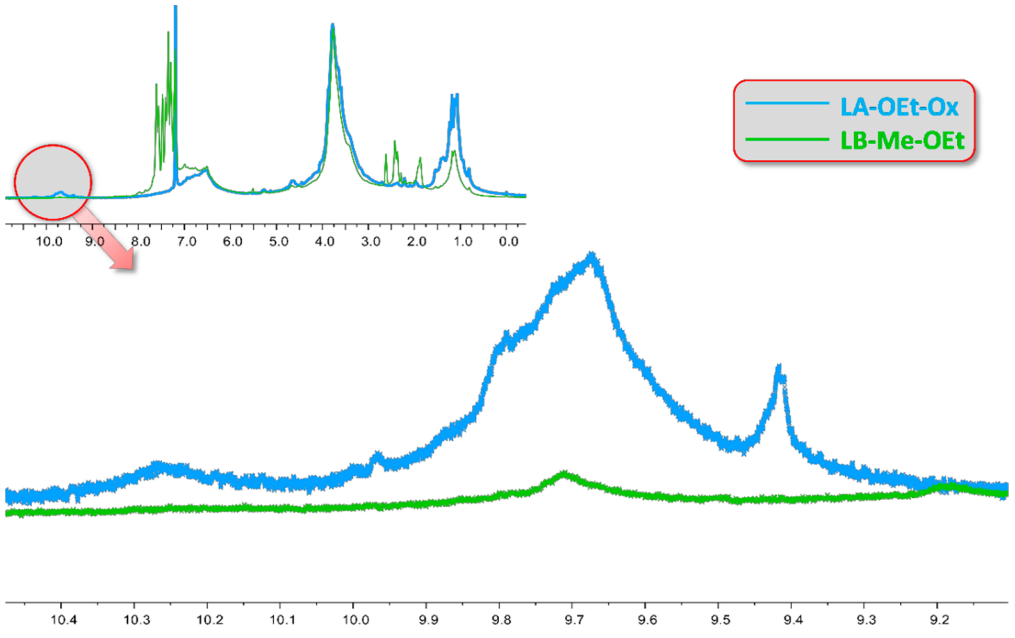

Figure 8. Overlay of the ^{1}H NMR spectra (600 MHz, $CDCl_3$) of **LA-OEt-Ox** and **LB-Me-OEt**.

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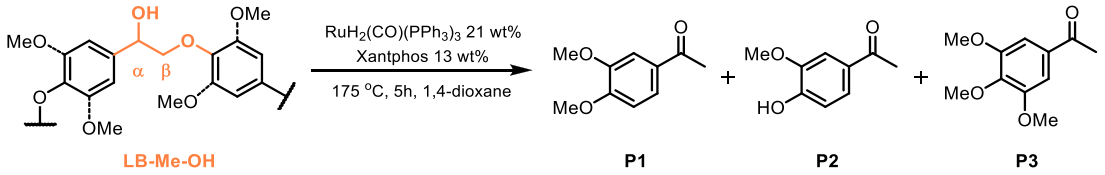
Scheme 1. Ru/Xantphos Catalyzed Hydrogen Neutral Depolymerization of Crude LB-Me-OH, Containing the Partly Defunctionalized α-Hydroxylation Lignin β-O-4 Motif B, To Give Acetophenone Derivatives (P1−P3)



oxidation step. After the oxidation step, the ratio increases to 2.2, which could indicate that the β-O-4 α-signal overlaps in **LA-Me-OEt-Ox** and **LB-Me-OEt** indicating that more β-O-4 linkage were broken or transformed to other unknown motifs in this modification step than expected based on the HSQC spectrum. This could also be seen in the resulting α:β-signal intensity ratio, which is back in the original order with a value of 1.67 after the α-hydroxylation step, where the α-signal shifts again. On the other hand, the $\beta-\beta$ signal stays constant throughout the modification steps, showing that this linking motif is unaffected (Table 2). Therefore, we concluded that **LB-Me-OEt** and **LB-Me-OH** had indeed formed but at the cost of a loss in the desired β-O-4 motif B. Based on the values for the β-O-4 β-signal, it can be clearly seen that the oxidation step is the problematic step, as half of the β-O-4 linkages is lost during this step. The significant decrease in molecular weight in the oxidation step indicate that oxidative cleavage occurs in this step (Figure S16). Also the α-hydroxylation caused a significant drop in β-O-4 linkages. This was unexpected as in previous literature[46,59] and in the above model compound reactions this step was straightforward. The ^{31}P NMR of the product after α-hydroxylation showed the clear reappearance of phenol moieties (Figure S17). This is clear evidence for β-O-4 linkage cleavage and explains the drop in β-O-4 content in this step. Additionally, these new signals could form from nonphenolic intermediates which have been formed in the oxidation step, as discussed in literature.[45]

Finally, the crude **LB-Me-OH** was subjected to hydrogen neutral depolymerization using Ru/Xantphos (Scheme 1). The HSQC NMR of the obtained crude product did show that the signals for the partly defunctionalized lignin β-O-4 motif B of **LB-Me-OH** had disappeared (Figure S19). The signals for the $\beta-\beta$ motif as well as the signal that overlapped with the α-signal of **LB-Me-OEt**, assigned to the unknown impurity did remain. Additionally, a weak signal that overlapped with the methyl groups of acetoveratrone (**P1**, 3,4-dimethoxy acetophenone) and acetovanillone (**P2**, 4-hydroxy-3-methoxy acetophenone) was observed, which could be a combination of monomeric depolymerization product as well as lignin end groups that are the results of C−O cleavage of the α-hydroxylated lignin β-O-4 motif B. GC-MS analysis of the low-molecular weight fraction of this depolymerization mixture obtained by toluene extraction did confirm that **P1** and **P2** had been formed, albeit in small amounts (Figure S21). Additionally, 3,4,5-trimethoxyacetophenone (**P3**) was found in the product mixture, which corresponds to the release of an S unit via C−O bond cleavage. The major product was **P1**, which originates from methylated phenolic G-type end-groups. Both **P1** and **P3** are likely the result of the release of methylated end-groups when an α-hydroxylated β-O-4 motif B located near the end of the chain is cleaved. While, for **P2** to be released, two of these linkages need to flank one monomeric unit inside the chain. The latter is relatively unlikely due to the low amount of linkages that remained after the sequential modification steps. The yields of **P1−P3** were low (<2 wt %, based on the amount of **LB-Me-OH**) which is due to the low amount of cleavable β-O-4 motif B in the lignin used as substrate (Table 2).

CONCLUSION

In this paper, a new approach to lignin depolymerization is presented, which shifts the emphasis from the depolymerization reaction itself to catalytic modification of the lignin structure to facilitate selective depolymerization that is otherwise not feasible. Here, sequential catalytic steps for the modification of the β-O-4 motif of lignin to a partly defunctionalized lignin are presented (78% yield over three steps starting from model compound **A-OEt**). The first step is the selective aerobic oxidation of the primary alcohol in the γ-position of the β-O-4 motif to the corresponding γ-aldehyde, which relied on "protection" of the benzylic α-hydroxyl group in the form of an ether to obtain a stable isolatable product. Where selective reactions on the γ-hydroxyl group were reported with α-butoxylated β-O-4,[46] for the first time in this work, this is achieved by making use of the α-ethoxylated β-O-4 motif that can be obtained from ethanosolv extraction of lignocellulosic biomass[60] which has been operating on an industrial scale. The second step defunctionalized the β-O-4 motif by removal of the aldehyde group by catalytic decarbonylation to release carbon monoxide using Rh/dppp and reaching near quantitative yield and selectivity. Finally, in the third step this partly defunctionalized β-O-4 motif was "deprotected" by exchanging the α-ethoxy group with an α-hydroxyl group. This allows for recycling of the ethanol that was consumed in the ethanosolv extraction by incorporation into the lignin structure. Overall, this novel catalytic modification sequence converts the native β-O-4 motif A to a partially defunctionalized β-O-4 motif B that represents the structure of "simplified" β-O-4 model compounds often used in catalyst development for lignin depolymerization as well as mechanistic studies hereof.[17] Thus, this methodology can allow for the lignin structure to be transformed into a structural motif for which many elegant catalytic procedures have been developed that have not necessary always proved effective for depolymerization of the native lignin structure. Here, this is exemplified by application of Ru/Xantphos catalyzed hydrogen neutral C−O bond cleavage, a procedure that was previously shown to work excellently for the simplified β-O-4 type model compound while being ineffective for native highly functionalized β-O-4 type model compounds. Indeed, excellent yields of over 90% of 3,4-dimethoxyacetophenone and guaiacol were obtained by application of this hydrogen borrowing protocol on the obtained defunctionalized β-O-4 motif. The modification steps used to obtain this defunctionalized β-O-4 motif were also demonstrated on walnut ethanosolv lignin with high α-ethoxy incorporation. An additional phenol methylation step

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proved to be essential to achieve effective conversion due to either solubility problems or interference of the phenols in the copper catalyzed aerobic oxidation reaction. Furthermore, the decarbonylation as well as the α-ethoxy "deprotection" were demonstrated on lignin. However, the modification steps were found to be less effective when applied on lignin compared to application on the model compounds. This was reflected in the significant loss of β-O-4 linkage over the modification sequence. Nevertheless, lignin containing the targeted defunctionalized β-O-4 motif was identified and could be depolymerized via hydrogen borrowing methodology to yield acetophenone derivatives. Future work will focus on optimizing the reaction sequence on lignin as well as potentially shortening the reaction sequence by application of dehydrogenative decarbonylation catalysts.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.9b01193.

Experimental procedures for the synthesis of model compounds; procedures for catalytic reactions; analytical procedures for NMR, GC-FID, GC-MS, and HPLC; analysis results; HSQC NMR data for the lignin (PDF)

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Author Contributions

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Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS

bpy = 2,2′-bipyridine; cod = 1,5-cyclooctadiene; DAIB = (diacetoxyiodo)benzene; DMSO = dimethyl sulfoxide; dppp = 1,3-bis(diphenylphosphino)propane; ES = external standard; GC-FID = gas chromatography with flame ionization detector; GC-MS = gas chromatography with mass spectrometry detector; GC-TCD = gas chromatography with a thermal conductivity detector; HPLC = High performance liquid chromatography; HSQC = heteronuclear single quantum coherence spectroscopy; IS = internal standard; MeCN = acetonitrile; NMI = 1-methylimidazole; PS-DAIB = polystyrene bound (diacetoxyiodo)benzene; TBAF = tetrabutylammonium fluoride; TEMPO = 2,2,6,6-tetramethylpiperidine 1-oxyl

■ REFERENCES

(1) Ferrini, P.; Rinaldi, R. Catalytic Biorefining of Plant Biomass to Non-Pyrolytic Lignin Bio-Oil and Carbohydrates through Hydrogen Transfer Reactions. *Angew. Chemie Int. Ed.* **2014**, *53* (33), 8634–8639.

(2) Li, C.; Zhao, X.; Wang, A.; Huber, G. W.; Zhang, T. Catalytic Transformation of Lignin for the Production of Chemicals and Fuels. *Chem. Rev.* **2015**, *115* (21), 11559–11624.

(3) Sun, Z.; Fridrich, B.; de Santi, A.; Elangovan, S.; Barta, K. Bright Side of Lignin Depolymerization: Toward New Platform Chemicals. *Chem. Rev.* **2018**, *118* (2), 614–678.

(4) Schutyser, W.; Renders, T.; Van Den Bosch, S.; Koelewijn, S. F.; Beckham, G. T.; Sels, B. F. Chemicals from Lignin: An Interplay of Lignocellulose Fractionation, Depolymerisation, and Upgrading. *Chem. Soc. Rev.* **2018**, *47* (3), 852–908.

(5) Tuck, C. O.; Pérez, E.; Horváth, I. T.; Sheldon, R. A.; Poliakoff, M. Valorization of Biomass: Deriving More Value from Waste. *Science* **2012**, *337* (6095), 695–699.

(6) Ragauskas, A. J.; Beckham, G. T.; Biddy, M. J.; Chandra, R.; Chen, F.; Davis, M. F.; Davison, B. H.; Dixon, R. A.; Gilna, P.; Keller, M. Lignin Valorization: Improving Lignin Processing in the Biorefinery. *Science* **2014**, *344* (6185), 1246843–1246843.

(7) Sun, Z.; Bottari, G.; Afanasenko, A.; Stuart, M. C. A.; Deuss, P. J.; Fridrich, B.; Barta, K. Complete Lignocellulose Conversion with Integrated Catalyst Recycling Yielding Valuable Aromatics and Fuels. *Nat. Catal.* **2018**, *1* (1), 82–92.

(8) Renders, T.; Van den Bosch, S.; Koelewijn, S.-F.; Schutyser, W.; Sels, B. F. Lignin-First Biomass Fractionation: The Advent of Active Stabilisation Strategies. *Energy Environ. Sci.* **2017**, *10* (7), 1551–1557.

(9) Shuai, L.; Amiri, M. T.; Questell-Santiago, Y. M.; Héroguel, F.; Li, Y.; Kim, H.; Meilan, R.; Chapple, C.; Ralph, J.; Luterbacher, J. S. Formaldehyde Stabilization Facilitates Lignin Monomer Production during Biomass Depolymerization. *Science* **2016**, *354* (6310), 329–333.

(10) Güvenatam, B.; Heeres, E. H. J.; Pidko, E. A.; Hensen, E. J. M. Lewis-Acid Catalyzed Depolymerization of Protobind Lignin in Supercritical Water and Ethanol. *Catal. Today* **2016**, *259* (Part 2), 460–466.

(11) Huang, X.; Zhu, J.; Korányi, T. I.; Boot, M. D.; Hensen, E. J. M. Effective Release of Lignin Fragments from Lignocellulose by Lewis Acid Metal Triflates in the Lignin-First Approach. *ChemSusChem* **2016**, *9* (23), 3261.

(12) Sun, J.; Li, H.; Xiao, L.-P.; Guo, X.; Fang, Y.; Sun, R.-C.; Song, G. Fragmentation of Woody Lignocellulose into Primary Monolignols and Their Derivatives. *ACS Sustainable Chem. Eng.* **2019**, *7*, 4666–4674.

(13) Monsigny, L.; Feghali, E.; Berthet, J. C.; Cantat, T. Efficient Reductive Depolymerization of Hardwood and Softwood Lignins with Brookhart's Iridium(III) Catalyst and Hydrosilanes. *Green Chem.* **2018**, *20* (9), 1981–1986.

(14) Zhang, B.; Qi, Z.; Li, X.; Ji, J.; Luo, W.; Li, C.; Wang, A.; Zhang, T. ReOxAC-Catalyzed Cleavage of C-O Bonds in Lignin Model Compounds and Alkaline Lignins. *ACS Sustainable Chem. Eng.* **2019**, *7* (1), 208–215.

(15) Bernt, C. M.; Manesewan, H.; Chui, M.; Boscolo, M.; Ford, P. C. Temperature Tuning the Catalytic Reactivity of Cu-Doped Porous Metal Oxides with Lignin Models. *ACS Sustainable Chem. Eng.* **2018**, *6* (2), 2510–2516.

DOI: 10.1021/acssuschemeng.9b01193
ACS Sustainable Chem. Eng. 2019, 7, 12105–12116

(16) Song, Q.; Wang, F.; Cai, J.; Wang, Y.; Zhang, J.; Yu, W.; Xu, J. Lignin Depolymerization (LDP) in Alcohol over Nickel-Based Catalysts via a Fragmentation-Hydrogenolysis Process. *Energy Environ. Sci.* **2013**, *6* (3), 994−1007.
(17) Deuss, P. J.; Barta, K. From Models to Lignin: Transition Metal Catalysis for Selective Bond Cleavage Reactions. *Coord. Chem. Rev.* **2016**, *306* (2), 510−532.
(18) Kim, S.; Chmely, S. C.; Nimlos, M. R.; Bomble, Y. J.; Foust, T. D.; Paton, R. S.; Beckham, G. T. Computational Study of Bond Dissociation Enthalpies for a Large Range of Native and Modified Lignins. *J. Phys. Chem. Lett.* **2011**, *2* (22), 2846−2852.
(19) Nguyen, J. D.; Matsuura, B. S.; Stephenson, C. R. J. A Photochemical Strategy for Lignin Degradation at Room Temperature. *J. Am. Chem. Soc.* **2014**, *136* (4), 1218−1221.
(20) Rahimi, A.; Azarpira, A.; Kim, H.; Ralph, J.; Stahl, S. S. Chemoselective Metal-Free Aerobic Alcohol Oxidation in Lignin. *J. Am. Chem. Soc.* **2013**, *135* (17), 6415−6418.
(21) Lancefield, C. S.; Ojo, O. S.; Tran, F.; Westwood, N. J. Isolation of Functionalized Phenolic Monomers through Selective Oxidation and C-O Bond Cleavage of the β-O-4 Linkages in Lignin. *Angew. Chem., Int. Ed.* **2015**, *54* (1), 258−262.
(22) Lan, W.; Amiri, M. T.; Hunston, C. M.; Luterbacher, J. S. Protection Group Effects During α,γ-Diol Lignin Stabilization Promote High-Selectivity Monomer Production. *Angew. Chemie Int. Ed.* **2018**, *57* (5), 1356−1360.
(23) Zhu, R.; Wang, B.; Cui, M.; Deng, J.; Li, X.; Ma, Y.; Fu, Y. Chemoselective Oxidant-Free Dehydrogenation of Alcohols in Lignin Using Cp*Ir Catalysts. *Green Chem.* **2016**, *18* (7), 2029−2036.
(24) Zhang, C.; Li, H.; Lu, J.; Zhang, X.; Macarthur, K. E.; Heggen, M.; Wang, F. Promoting Lignin Depolymerization and Restraining the Condensation via an Oxidation-Hydrogenation Strategy. *ACS Catal.* **2017**, *7* (5), 3419−3429.
(25) Wang, M.; Zhang, X.; Li, H.; Lu, J.; Liu, M.; Wang, F. Carbon Modification of Nickel Catalyst for Depolymerization of Oxidized Lignin to Aromatics. *ACS Catal.* **2018**, *8* (2), 1614−1620.
(26) Doble, M. V.; Jarvis, A. G.; Ward, A. C. C.; Colburn, J. D.; Götze, J. P.; Bühl, M.; Kamer, P. C. J. Artificial Metalloenzymes as Catalysts for Oxidative Lignin Degradation. *ACS Sustainable Chem. Eng.* **2018**, *6* (11), 15100−15107.
(27) Nichols, J. M.; Bishop, L. M.; Bergman, R. G.; Ellman, J. A. Catalytic C-O Bond Cleavage of 2-Aryloxy-1-Arylethanols and Its Application to the Depolymerization of Lignin-Related Polymers. *J. Am. Chem. Soc.* **2010**, *132* (36), 12554−12555.
(28) Yan, T.; Feringa, B. L.; Barta, K. Iron Catalysed Direct Alkylation of Amines with Alcohols. *Nat. Commun.* **2014**, *5*, 5602.
(29) Elangovan, S.; Neumann, J.; Sortais, J. B.; Junge, K.; Darcel, C.; Beller, M. Efficient and Selective N-Alkylation of Amines with Alcohols Catalysed by Manganese Pincer Complexes. *Nat. Commun.* **2016**, *7* (1), 12641.
(30) Reed-Berendt, B. G.; Polidano, K.; Morrill, L. C. Recent Advances in Homogeneous Borrowing Hydrogen Catalysis Using Earth-Abundant First Row Transition Metals. *Org. Biomol. Chem.* **2019**, *17* (7), 1595−1607.
(31) Corma, A.; Navas, J.; Sabater, M. J. Advances in One-Pot Synthesis through Borrowing Hydrogen Catalysis. *Chem. Rev.* **2018**, *118* (4), 1410−1459.
(32) Rahimi, A.; Ulbrich, A.; Coon, J. J.; Stahl, S. S. Formic-Acid-Induced Depolymerization of Oxidized Lignin to Aromatics. *Nature* **2014**, *515* (7526), 249−252.
(33) Lahive, C. W.; Deuss, P. J.; Lancefield, C. S.; Sun, Z.; Cordes, D. B.; Young, C. M.; Tran, F.; Slawin, A. M. Z.; de Vries, J. G.; Kamer, P. C. J.; et al. Advanced Model Compounds for Understanding Acid-Catalyzed Lignin Depolymerization: Identification of Renewable Aromatics and a Lignin-Derived Solvent. *J. Am. Chem. Soc.* **2016**, *138* (28), 8900−8911.
(34) Dabral, S.; Mottweiler, J.; Rinesch, T.; Bolm, C. Base-Catalysed Cleavage of Lignin β-O-4 Model Compounds in Dimethyl Carbonate. *Green Chem.* **2015**, *17* (11), 4908−4912.
(35) Deuss, P. J.; Scott, M.; Tran, F.; Westwood, N. J.; de Vries, J. G.; Barta, K. Aromatic Monomers by in Situ Conversion of Reactive Intermediates in the Acid-Catalyzed Depolymerization of Lignin. *J. Am. Chem. Soc.* **2015**, *137* (23), 7456−7467.
(36) Wu, A.; Patrick, B. O.; Chung, E.; James, B. R. Hydrogenolysis of β-O-4 Lignin Model Dimers by a Ruthenium-Xantphos Catalyst. *Dalt. Trans.* **2012**, *41* (36), 11093−11106.
(37) Luo, J.; Zhang, X.; Lu, J.; Zhang, J. Fine Tuning the Redox Potentials of Carbazolic Porous Organic Frameworks for Visible-Light Photoredox Catalytic Degradation of Lignin β-O-4 Models. *ACS Catal.* **2017**, *7* (8), 5062−5070.
(38) Ren, Y.; Yan, M.; Wang, J.; Zhang, Z. C.; Yao, K. Selective Reductive Cleavage of Inert Aryl C-O Bonds by an Iron Catalyst. *Angew. Chem. - Int. Ed.* **2013**, *52* (48), 12674−12678.
(39) Zhou, X.; Mitra, J.; Rauchfuss, T. B. Lignol Cleavage by Pd/C under Mild Conditions and without Hydrogen: A Role for Benzylic C-H Activation? *ChemSusChem* **2014**, *7* (6), 1623−1626.
(40) Galkin, M. V.; Sawadjoon, S.; Rohde, V.; Dawange, M.; Samec, J. S. M. Mild Heterogeneous Palladium-Catalyzed Cleavage of β-o-4′-Ether Linkages of Lignin Model Compounds and Native Lignin in Air. *ChemCatChem* **2014**, *6* (1), 179−184.
(41) vomStein, T.; Weigand, T.; Merkens, C.; Klankermayer, J.; Leitner, W. Trimethylenemethane-Ruthenium(II)-Triphos Complexes as Highly Active Catalysts for Catalytic C-O Bond Cleavage Reactions of Lignin Model Compounds. *ChemCatChem* **2013**, *5* (2), 439−441.
(42) Shaw, L.; Somisara, D. M. U. K.; How, R. C.; Westwood, N. J.; Bruijnincx, P. C. A.; Weckhuysen, B. M.; Kamer, P. C. J. Electronic and Bite Angle Effects in Catalytic C-O Bond Cleavage of a Lignin Model Compound Using Ruthenium Xantphos Complexes. *Catal. Sci. Technol.* **2017**, *7* (3), 619−626.
(43) Olsen, E. P. K.; Madsen, R. Iridium-Catalyzed Dehydrogenative Decarbonylation of Primary Alcohols with the Liberation of Syngas. *Chem. - Eur. J.* **2012**, *18* (50), 16023−16029.
(44) Dabral, S.; Hernández, J. G.; Kamer, P. C. J.; Bolm, C. Organocatalytic Chemoselective Primary Alcohol Oxidation and Subsequent Cleavage of Lignin Model Compounds and Lignin. *ChemSusChem* **2017**, *10* (13), 2707−2713.
(45) Lancefield, C. S.; Teunissen, L. W.; Weckhuysen, B. M.; Bruijnincx, P. C. A. Iridium-Catalysed Primary Alcohol Oxidation and Hydrogen Shuttling for the Depolymerisation of Lignin. *Green Chem.* **2018**, *20* (14), 3214−3221.
(46) Panovic, I.; Lancefield, C. S.; Phillips, D.; Gronnow, M.; Westwood, N. J. Selective Primary Oxidation of Lignin Streams from Butanol-Pretreated Agricultural Waste Biomass. *ChemSusChem* **2018**, *12* (2), 542−548.
(47) Hoover, J. M.; Steves, J. E.; Stahl, S. S. Copper(I)/Tempo-Catalyzed Aerobic Oxidation of Primary Alcohols to Aldehydes with Ambient Air. *Nat. Protoc.* **2012**, *7* (6), 1161−1166.
(48) Hoover, J. M.; Stahl, S. S. Highly Practical Copper(I)/TEMPO Catalyst System for Chemoselective Aerobic Oxidation of Primary Alcohols. *J. Am. Chem. Soc.* **2011**, *133* (42), 16901−16910.
(49) Hoover, J. M.; Ryland, B. L.; Stahl, S. S. Mechanism of Copper(I)/TEMPO-Catalyzed Aerobic Alcohol Oxidation. *J. Am. Chem. Soc.* **2013**, *135* (6), 2357−2367.
(50) Doughty, D. H.; Anderson, M. P.; Casalnuovo, A. L.; McGuiggan, M. F.; Tso, C. C.; Wang, H. H.; Pignolet, L. H. The Effect of Chelating Diphosphine Ligands on Homogeneous Catalytic Decarbonylation Reactions Using Cationic Rhodium Catalysts. *Adv. Chem.* **1982**, *196*, 65−83.
(51) Doughty, D. H.; Pignolet, L. H. Catalytic Decarbonylation of Aldehydes. *J. Am. Chem. Soc.* **1978**, *100* (22), 7083−7085.
(52) De Mico, A.; Vescovi, A.; Margarita, R.; Parlanti, L.; Piancatelli, G. A Versatile and Highly Selective Hypervalent Iodine (III)/2,2,6,6-Tetramethyl-1-Piperidinyloxyl-Mediated Oxidation of Alcohols to Carbonyl Compounds. *J. Org. Chem.* **1997**, *62* (20), 6974−6977.
(53) Kärkäs, M. D.; Matsuura, B. S.; Monos, T. M.; Magallanes, G.; Stephenson, C. R. J. Transition-Metal Catalyzed Valorization of

DOI: 10.1021/acssuschemeng.9b01193
ACS Sustainable Chem. Eng. 2019, 7, 12105−12116

Lignin: The Key to a Sustainable Carbon-Neutral Future. *Org. Biomol. Chem.* **2016**, *14* (6), 1853−1914.
(54) Vangeel, T.; Schutyser, W.; Renders, T.; Sels, B. F. Perspective on Lignin Oxidation: Advances, Challenges, and Future Directions. *Top. Curr. Chem.* **2018**, *376* (4), 30.
(55) vom Stein, T.; den Hartog, T.; Buendia, J.; Stoychev, S.; Mottweiler, J.; Bolm, C.; Klankermayer, J.; Leitner, W. Ruthenium-Catalyzed C-C Bond Cleavage in Lignin Model Substrates. *Angew. Chem., Int. Ed. Engl.* **2015**, *54* (20), 5859−5863.
(56) Lancefield, C. S.; Panovic, I.; Deuss, P. J.; Barta, K.; Westwood, N. J. Pre-Treatment of Lignocellulosic Feedstocks Using Biorenewable Alcohols: Towards Complete Biomass Valorisation. *Green Chem.* **2017**, *19* (1), 202−214.
(57) Panovic, I.; Montgomery, J. R. D.; Lancefield, C. S.; Puri, D.; Lebl, T.; Westwood, N. J. Grafting of Technical Lignins through Regioselective Triazole Formation on β-O-4 Linkages. *ACS Sustainable Chem. Eng.* **2017**, *5* (11), 10640−10648.
(58) Arato, C.; Pye, E. K.; Gjennestad, G. The Lignol Approach to Biorefining of Woody Biomass to Produce Ethanol and Chemicals. *Appl. Biochem. Biotechnol.* **2005**, *123* (1−3), 0871−0882.
(59) Zijlstra, D. S.; de Vries, J.; Oldenburger, B.; Barta, K.; de Santi, A.; Deuss, P. J. Extraction of Lignin with High β-O-4 Content by Mild Ethanol Extraction and Its Effect on the Depolymerization Yield. *J. Vis. Exp.* **2019**, No. 143, e58575.
(60) Bauer, S.; Sorek, H.; Mitchell, V. D.; Ibáñez, A. B.; Wemmer, D. E. Characterization of Miscanthus Giganteus Lignin Isolated by Ethanol Organosolv Process under Reflux Condition. *J. Agric. Food Chem.* **2012**, *60* (33), 8203−8212.
(61) Beejapur, H. A.; Zhang, Q.; Hu, K.; Zhu, L.; Wang, J.; Ye, Z. TEMPO in Chemical Transformations: From Homogeneous to Heterogeneous. *ACS Catal.* **2019**, *9*, 2777−2830.
(62) Cao, Q.; Dornan, L. M.; Rogan, L.; Hughes, N. L.; Muldoon, M. J. Aerobic Oxidation Catalysis with Stable Radicals. *Chem. Commun.* **2014**, *50* (35), 4524−4543.
(63) Iwai, T.; Fujihara, T.; Tsuji, Y. The Iridium-Catalyzed Decarbonylation of Aldehydes under Mild Conditions. *Chem. Commun.* **2008**, *0* (46), 6215−6217.
(64) Jastrzebski, R.; Constant, S.; Lancefield, C. S.; Westwood, N. J.; Weckhuysen, B. M.; Bruijnincx, P. C. A. Tandem Catalytic Depolymerization of Lignin by Water-Tolerant Lewis Acids and Rhodium Complexes. *ChemSusChem* **2016**, *9* (16), 2074−2079.
(65) Deuss, P. J.; Lahive, C. W.; Lancefield, C. S.; Westwood, N. J.; Kamer, P. C. J.; Barta, K.; de Vries, J. G. Metal Triflates for the Production of Aromatics from Lignin. *ChemSusChem* **2016**, *9* (20), 2974−2981.
(66) Yokoyama, T. Revisiting the Mechanism of β-O-4 Bond Cleavage During Acidolysis of Lignin. Part 6: A Review. *J. Wood Chem. Technol.* **2015**, *35*, 27−42.
(67) Sturgeon, M. R.; Kim, S.; Lawrence, K.; Paton, R. S.; Chmely, S. C.; Nimlos, M.; Foust, T. D.; Beckham, G. T. A Mechanistic Investigation of Acid-Catalyzed Cleavage of Aryl-Ether Linkages: Implications for Lignin Depolymerization in Acidic Environments. *ACS Sustainable Chem. Eng.* **2014**, *2* (3), 472−485.
(68) Lu, F.; Ralph, J. Non-Degradative Dissolution and Acetylation of Ball-Milled Plant Cell Walls: High-Resolution Solution-State NMR. *Plant J.* **2003**, *35* (4), 535−544.
(69) Miles-Barrett, D. M.; Montgomery, J. R. D.; Lancefield, C. S.; Cordes, D. B.; Slawin, A. M. Z.; Lebl, T.; Carr, R.; Westwood, N. J. Use of Bisulfite Processing to Generate High-β-O-4 Content Water-Soluble Lignosulfonates. *ACS Sustainable Chem. Eng.* **2017**, *5* (2), 1831−1839.
(70) Constant, S.; Frissen, A. E.; Boelens, R.; Wienk, H. L. J.; Peinder, P.; Gosselink, R. J. A.; Huijgen, W. J. J.; van Es, D. S.; Grisel, R. J. H.; Bruijnincx, P. C. A.; et al. New Insights into the Structure and Composition of Technical Lignins: A Comparative Characterisation Study. *Green Chem.* **2016**, *18* (9), 2651−2665.
(71) Cui, C.; Sadeghifar, H.; Sen, S.; Argyropoulos, D. S. Toward Thermoplastic Lignin Polymers; Part II: Thermal & Polymer Characteristics of Kraft Lignin & Derivatives. *BioResources* **2012**, *8* (1), 864−886.
(72) Sen, S.; Patil, S.; Argyropoulos, D. S. Methylation of Softwood Kraft Lignin with Dimethyl Carbonate. *Green Chem.* **2015**, *17* (2), 1077−1087.

DOI: 10.1021/acssuschemeng.9b01193
ACS Sustainable Chem. Eng. 2019, 7, 12105−12116